UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

MJ

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/347,496	07/02/99	XU	J 21021.471C1

000500 HM12/0605
SEED INTELLECTUAL PROPERTY LAW GROUP PLL
701 FIFTH AVE
SUITE 6300
SEATTLE WA 98104-7092

EXAMINER	
SOUAYA, I	
ART UNIT	**PAPER NUMBER**
1655	15

DATE MAILED: 06/05/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/347,496	Jiangchun Xu
Examiner	**Art Unit**
Jehanne Souaya	1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Mar 22, 2001* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-78* is/are pending in the application.

4a) Of the above, claim(s) *1-64 and 71-75* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *65-70 and 76-78* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 6

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group XII and SEQ ID NO 21 in Paper No.13 is acknowledged. The traversal is on the ground(s) that it would not be an undue burden for the examiner to search additional claims and/or species. This is not found persuasive because the inventions are patentably distinct as stated in the restrictions mailed 9/11/00 and 12/14/00. The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 101

2. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. Claims 65-70 and 76-78 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility.

The claims are drawn to methods of determining the presence or absence of cancer and determining the progression cancer based on expression levels of a colon tumor protein encoded by a sequence comprising SEQ ID NO 21. The claims are further drawn to the

polynucleotides comprising an oligonucleotide of 10-40 nucleotides that hybridizes under moderately stringent conditions to a colon tumor protein comprising an amino acid sequence encoded by SEQ ID NO 21.

The specification teaches performing PCR based subtraction to identify clones that were overexpressed in colon cancer than in normal tissue (p. 50). The specification teaches that clones that showed two or more fold expression in colon tumor group as compared to normal tissue were sequences and analyzed for homology to other known genes. The specification teaches that SEQ ID NO 21 shows homology to L1 cadherin. It is known for nucleic acids as well as proteins, for example, that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. Therefore, the citation of sequence homology results in an unpredictable and therefore unreliable correspondence between the claimed biomolecule and the indicated similar biomolecule and therefore lacks support regarding utility. (See Russell et al, J. Mol. Biol. Vol. 244, 1994, pp 332-350, who teaches that the results of an analysis of side chain to side chain secondary structure and accessibility between related proteins suggest that there is little in common between distantly related protein structures and that secondary structure lengths and loops in distantly related structures vary substantially- p. 345).

The specification does not teach of a diagnostic study which correlates the overexpression of SEQ ID NO 21 with colon cancer or family of cancer as the specification teaches that 3/6

normal tissue samples showed overexpression of SEQ ID NO 21. The specification does not teach a function for the polypeptide encoded by SEQ ID NO 21, or how such a putative polypeptide is associated with any cancer. The polynucleotides of the present invention could generally be used to detect themselves, and to encode polypeptides. However, the specification fails to disclose a specific asserted utility for the polynucleotides of the claimed invention. The specification also fails to disclose a specific asserted utility for probes and primers because the use of polynucleotides as probes and primers is generally applicable to any nucleic acid and is therefore not particular to the oligonucleotides of the claimed invention. Although the probes and primers can be used to detect the polynucleotides of the claimed invention, the specification sets forth no specific function of the polynucleotides of the claimed invention. Therefore, identifying and/or studying the sequences of the claimed invention does not define "a real world" context of use. The oligonucleotides of the claimed invention are only useful for detecting the polynucleotides of the claimed invention. Because the claimed invention is not supported by a specific and substantial asserted utility for the reasons set forth above, one skilled in the art would not recognize a utility for the claimed invention.

Claim Rejections - 35 USC § 112

Enablement

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 65-70 and 76-78 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

5. Claims 65-70 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are broadly drawn to a method for determining the presence or absence of any cancer in a patient by detecting hybridization between an oligonucleotide that hybridizes to a polynucleotide that encodes a colon tumor protein of SEQ ID NO 21 and comparing the amount with a predetermined cutoff value, and therefrom determining the presence or absence of cancer in a patient. The claims are also broadly drawn to monitoring the progression of cancer in a patient. The specification teaches that SEQ ID NO 21 is a contig, however the specification has not taught the full length cDNA sequence which is encompassed by SEQ ID NO 21, nor the full length protein encoded by this cDNA sequence. The specification has also not taught the function of the colon tumor protein encoded by SEQ ID NO 21. While the specification has taught that

SEQ ID NO 21 shows homology to L1-cadherin, the specification does not teach the degree of homology. The specification further does not teach the function of L1-cadherin nor why a protein possessing such homology would be implicated in colon cancer. It is known for nucleic acids as well as proteins, for example, that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. Therefore, the citation of sequence homology results in an unpredictable and therefore unreliable correspondence between the claimed biomolecule and the indicated similar biomolecule and therefore lacks support regarding enablement. (See Russell et al, J. Mol. Biol. Vol. 244, 1994, pp 332-350, who teaches that the results of an analysis of side chain to side chain secondary structure and accessibility between related proteins suggest that there is little in common between distantly related protein structures and that secondary structure lengths and loops in distantly related structures vary substantially- p. 345).

The specification, teaches that SEQ ID NO 21 showed over-expression in about half of colon tumors and low level overexpression in 3/6 normal colon tissue. The specification however, fails to teach how much expression was detected, and provides no guidance for the skilled artisan to determine the difference between over expression and "low level over expression". The claims instead provide that the skilled artisan must compare the amount of SEQ ID NO 21 with the amount of amplified DNA indicative of the presence or absence of cancer so as to determine the presence or absence of cancer in a patient, which constitutes undue experimentation. The

specification does not provide guidance as to what the amount of DNA is that is indicative of the presence or absence of cancer. Without such guidance, the skilled artisan would have to perform a broad study of patients with different types of cancer whereby the level of SEQ ID NO 21 expression in patients with cancer would have to be determined first, before a particular level of expression could be correlated with the presence or absence of cancer. As the specification offers no guidance evidence as to the correlation between SEQ ID NO 21 expression and cancer, and further teaches that 3/6 colon tumor showed "low level over expression" of SEQ ID NO 21, the results of such a study would be unpredictable, thus constituting undue experimentation.

With regard to determining the progression of cancer in a patient, the specification, teaches that SEQ ID NO 21 showed over-expression in about half of colon tumors and low level overexpression in 3/6 normal colon tissue. The specification however, fails to teach how much expression was detected and also does not provide a level of comparison for the skilled artisan to determine progression of cancer. The specification offers no data to correlate amount of SEQ ID NO 21 expression with a particular stage of cancer, and the claims instead provide that the skilled artisan must compare the amount of SEQ ID NO 21 with the amount of amplified DNA indicative of each stage of cancer so as to determine the progression of cancer in a patient, which constitutes undue experimentation. The specification does not provide guidance as to what the amount of DNA is that is indicative of a particular stage of cancer. Without such guidance, the skilled artisan would have to perform a broad study of patients at different levels of progression of cancer whereby the level of SEQ ID NO 21 expression in patients with cancer would have to be

determined first, before a particular level of expression could be correlated with a particular stage of cancer. As the specification offers no guidance evidence as to the correlation between SEQ ID NO 21 expression and stages of cancer, the skilled artisan would be required to practice undo experimentation to determine the progression cancer in a patient.

The art is unpredictable as to diagnosing cancer based on the presence or absence of a gene. Sidransky (Int. J. Cancer, vol. 64, pp 1-2, 1995) teaches that neoplasms arise and progress through the accumulation of various genetic changes (p. 1, para 2) in protooncogenes and tumor suppressor genes. Sidransky teaches that the average number of genetic events that occurs in an individual cell prior to detection of a clinical tumor varies from one cancer type to another and that it is the accumulation of these events and not necessarily their precise order that leads to progression. Sidransky teaches that because genetic alterations are an intimate part of cancer progression, they can serve as markers for their detection (p. 1, para 4). Sidransky further teaches that the value of these studies is predicated on the selection of appropriate markers and the application of appropriate technology. One of the requirements taught by Sidransky involves acquiring the primary tissue from affected population to demonstrate the efficacy of these particular markers (p.2, para.4). Sidransky teaches that for early detection, molecular markers to augment cytologic diagnosis and assess patients may include the identification of specific genetic alterations such as clonal markers, gene mutations, and other molecular abnormalities in bodily fluids.

Therefore, based on the lack of guidance from the specification and the unpredictability of the art with regard to diagnosing cancer based on the presence or absence of a single gene, the skilled artisan would require undue experimentation to make or use the invention as claimed. It is further noted that the art does not the protein encoded by SEQ ID NO 21, nor the detection of cancer based on a certain level of expression of this protein. While this alone does not provide for non-enablement, such a teaching would aid in remedying the lack of guidance in the specification as to detecting the presence or absence of cancer in a patient based on the level of expression of SEQ ID NO 21. To practice the invention as claimed, the skilled artisan would have to perform trial and error, the results of which would be unpredictable, which is considered undue experimentation.

6. Claims 76-78 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an oligonucleotide consisting of 10 to 40 nucleotides that hybridize under highly stringent conditions to the polynucleotide of SEQ ID NO 21, does not reasonably provide enablement for an oligonucleotide comprising 10-40 nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes any colon tumor protein wherein the colon tumor protein comprises an amino acid sequence that is encoded by the polynucleotide of SEQ ID NO 21. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The claims are broadly drawn to an oligonucleotide that comprises 10-40 nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes a colon tumor protein wherein the colon tumor protein comprises an amino acid sequence that is encoded by the polynucleotide of SEQ ID NO 21. The open language "comprising" encompasses nucleic acids that are greater than 10-40 nucleotides. The claims are therefore drawn to nucleic acids that contain genomic sequences as well as the full open reading frame of the polypeptide encoded by SEQ ID NO 21. The recitation of such open language "comprising" and the recitation of moderately stringent conditions thus encompasses every mutant, homolog, functional fragment and allelic variant of SEQ ID NO 21 from any source. The specification, however, has taught that SEQ ID NO 21 is a contig. The specification has not taught the full length cDNA sequence which is encompassed by SEQ ID NO 21, nor the full length protein encoded by this cDNA sequence. The specification does not teach any mutants, homologues or allelic variants of such. It is well established that to claim a chemical compound, such as a polynucleotide, the inventor must be able to define the compound so as to distinguish the compound from other materials. The claimed compound must be defined in terms so as to provide a permanent and definite idea of the complete and operative invention. In the instant case, the claimed polynucleotides have not been clearly defined in terms of structure and function, and therefore one cannot make and use the polynucleotides as claimed. As stated in Vaek (CAFC 20 USPQ2d 1438, the "specification must teach those of skill in the art how to make and use the invention as broadly as it is claimed."

However, in order to be able to make an invention, one must be able to clearly define that invention.

Neither the specification nor the claims set forth any functional characteristics that are specific to the colon tumor protein that is encoded by SEQ ID NO 21 (nor whether such a polypeptide is a full length functional protein) that a skilled artisan could use to identify polynucleotides that constitute the colon tumor polypeptide encoded by SEQ ID NO 21 from other related molecules, other than those described by SEQ ID NO. That is, it is unpredictable as to how the skilled artisan could modify the polypeptide encoded by SEQ ID NO 21 without altering it's biological activity. It is noted that the specification teaches that SEQ ID NO 21 shows homology to L1-cadherin, however the function of this polypeptide is not taught, nor is it's possible role in colon carcinogenesis. It is known for nucleic acids as well as proteins, for example, that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. Therefore, the citation of sequence homology results in an unpredictable and therefore unreliable correspondence between the claimed biomolecule and the indicated similar biomolecule and therefore lacks support regarding enablement. (See Russell et al, J. Mol. Biol. Vol. 244, 1994, pp 332-350, who teaches that the results of an analysis of side chain to side chain secondary structure and accessibility between related proteins suggest that there is little in common between distantly

related protein structures and that secondary structure lengths and loops in distantly related structures vary substantially- p. 345).

In addition, in teaching the nucleic acid sequences of SEQ ID NOS 21, applicant has not taught the isolation of a representative number of polynucleotides that fall within the scope of the large genus encompassed by the instant claims. Thus, while the teachings of the specification and of the prior art would enable a skilled artisan to make and use polynucleotides consisting of 10-40 nucleotides that hybridize under highly stringent conditions to SEQ ID NO 21, it is unpredictable as to whether a skilled artisan could make and use an oligonucleotide comprising 10-40 nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes any colon tumor protein wherein the colon tumor protein comprises an amino acid sequence that is encoded by the polynucleotide of SEQ ID NO 21 It would require undue experimentation for a skilled artisan to make and use the invention as broadly as it is claimed.

Written Description

7. Claims 76-78 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to an oligonucleotide that comprises 10-40 nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes a colon tumor

protein wherein the colon tumor protein comprises an amino acid sequence that is encoded by the polynucleotide of SEQ ID NO 21. The open language "comprising" encompasses nucleic acids that are greater than 10-40 nucleotides. The claims are therefore drawn to nucleic acids that contain genomic sequences as well as the full open reading frame of the polypeptide encoded by SEQ ID NO 21. The recitation of such open language "comprising" and the recitation of moderately stringent conditions thus encompasses every mutant, homolog, functional fragment and allelic variant of SEQ ID NO 21 from any source. The specification, however, has taught that SEQ ID NO 21 is a contig. The specification has not taught the full length cDNA sequence which is encompassed by SEQ ID NO 21, nor the full length protein encoded by this cDNA sequence. The specification does not teach any mutants, homologues or allelic variants of such. Neither the specification nor the claims set forth any functional characteristics that are specific to the colon tumor protein that is encoded by SEQ ID NO 21 (nor whether such a polypeptide is a full length functional protein) that a skilled artisan could use to identify polynucleotides that constitute the colon tumor polypeptide encoded by SEQ ID NO 21 from other related molecules, other than those described by SEQ ID NO. In addition, in teaching the nucleic acid sequences of SEQ ID NOS 21, applicant has not taught the isolation of a representative number of polynucleotides that fall within the scope of the large genus encompassed by the instant claims. The claimed invention is drawn to a broad genus for which a representative number of sequences for each genus must be disclosed to meet the written description requirement of 112/1st paragraph. As set forth by the Court in *Vas Cath Inc. V. Mahurkar,* 19 USPQ2d 1111, the

written description must convey to one of skill in the art "with reasonable clarity" that as of the filing date applicant was in possession of the claimed invention. There is not adequate description of the genus polynucleotides encompassed by the instant claims. One of skill in the art would conclude that applicant was not in possession of the claimed nucleic acid sequences because the description of SEQ ID NO 21 is of only 1 member of the possible nucleic acids that belong to this genus of possible colon tumor protein and is not representative of the homologs, variants, mutants and to the genomic sequences that contain these homologs, variants, and mutants to support the claims.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

9. Claims 76-77 are rejected under 35 U.S.C. 102(b) as being anticipated by accession number Z67986.

Accession number Z67986 teaches a sequence that comprises 15 nucleotides of SEQ ID NO 21. As the claims read "an oligonucleotide comprising 10 to 40 nucleotides that hybridize under moderately stringent conditions...", the claims are being interpreted to encompasses any nucleic acid sequence that comprises 10-40 nucleotides, wherein the 10-40 nucleotides have the ability to hybridize under moderately stringent conditions. As the sequence taught in accession

number Z67986 contains 15 nucleotides that are identical to SEQ ID NO 21, the claims are encompassed by the teaching of accession number Z67986 as these 15 nucleotides would be able to hybridize to SEQ ID NO 21 under moderately stringent conditions.

10. No claims are allowable.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703)308-6565. The examiner can normally be reached Monday-Thursday from 7:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

LISA B. ARTHUR
PRIMARY EXAMINER
GROUP ~~1800~~ 1600

Jehanne Souaya
Patent examiner
May 31, 2001